Embark Veterinary Veterinary Practice

Swab code: seymour1010_swab
Swab activated on 7/1/2022
Results completed on 7/1/2022
Report accessed on 7/1/2022
Ordered by Lorenz Connelly

vetsupport@embarkvet.com
1-855-203-8271

Patient Information

Seymour

13 yrs 1 mths - NM
Genetic Age: 96 human years
Predicted Adult Weight: 62 lbs

Client Information

Mary Sullivan

mjs@example.com
555-555-0598

Breed Information

48.4% American Staffordshire Terrier
12.8% Golden Retriever
12.2% German Shepherd Dog
11.9% Boxer
8.6% Chinese Shar-Pei
6.1% English Cocker Spaniel

1 Increased Risk Result

MDR1 Drug Sensitivity Page 2

1 Notable Result

Degenerative Myelopathy, DM Page 7

218 Clear Results

Seymour is not at increased risk for 218 of the genetic health variants that Embark tests. Page 8

Glossary Page 24

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1 Increased Risk Result

MDR1 Drug Sensitivity

How to interpret this result

Seymour has one copy of this codominant variant in the ABCB1 gene. Dogs that inherit two abnormal copies (homozygous) will produce no normal p-glycoprotein and will be most strongly affected. Dogs that inherit only one abnormal copy of the ABCB1 gene (heterozygous) can show some effects though they will be less severely impacted because some normal p-glycoprotein will still be produced.

You can learn more about penetrance and care for Seymour below or email vetsupport@embarkvet.com should you desire to speak with a genetic counselor.

What is MDR1 Drug Sensitivity?

P-glycoprotein (P-gp), encoded by the ABCB1 gene (formerly known as the MDR1 gene, and the condition is still referred to as Multidrug Resistance 1), is a membrane transport protein in the ATP-binding cassette superfamily. P-gp is normally expressed in various mammalian tissues including apical (luminal) membranes of epithelial cells lining the lower gastrointestinal tract, brain capillary endothelial cells, biliary canalicular cells, brush border of renal proximal tubules, placenta, and testes. P-gp limits drug absorption in the gastrointestinal tract and promotes drug elimination in the liver, kidneys, and intestine. Furthermore, P-gp restricts drug uptake into cells and tissues, in particular their permeation across the blood-brain barrier. Taken altogether, P-gp has an important protective function for the organism by eliminating potentially toxic compounds from the body and preventing their entry into the brain and organs of reproduction.

Because of the predominant role of P-gp in drug disposition, mutation of the ABCB1 gene alters the pharmacokinetic properties of P-gp transported drugs, leading to enhanced oral bioavailability and reduced drug elimination through the liver, kidneys, and gut. Moreover, the brain penetration of P-gp transported drugs is increased and in many cases provokes neurological toxicity.

Variant Info

ABCB1

Codominant inheritance

1 copy of the variant

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Age of Onset of Clinical Signs or Symptoms

MDR1 drug sensitivity often presents in young adulthood, only because this is most commonly when a dog is first exposed to a problem drug like high dose ivermectin or acepromazine.

Clinical Signs

Symptoms arise after a dog has received an MDR1 problem drug or dosage and can range from vomiting and diarrhea to weakness, lethargy, ataxia, disorientation, tremors, seizures, blindness, or coma.

Penetrance and Additional Impact on Phenotype

Interestingly, research indicates that all dogs with this variant in ABCB1 are descendants of a dog that lived in Great Britain before the genetic isolation of breeds by registry (ca. 1873). Dogs that inherit two abnormal copies (homozygous) will produce no normal p-glycoprotein and will be most strongly affected. Dogs that inherit only one abnormal copy of the MDR1 gene (heterozygous) can show some effects though they will be less severely impacted because some normal p-glycoprotein will still be produced.

Of note, several commonly used drugs can inhibit P-glycoprotein function, even in animals with normal ABCB1 gene structure. Consequently, veterinarians may encounter dogs and cats with intrinsic (genetically mediated) P-glycoprotein dysfunction, as well as with extrinsic, or acquired, P-glycoprotein dysfunction (animals receiving a drug that inhibits P-glycoprotein function). In ABCB1 wild-type (normal) dogs, ketoconazole and spinosad are most often associated with severe adverse effects because of their ability to inhibit P-glycoprotein function.

Approximate frequency for select breeds (from WSU):

- Australian Shepherd 50%
- Australian Shepherd Mini 50%
- Chinook 25%
- Collie 70%
- English Shepherd 15%
- German Shepherd Dog 10%
- Long-haired Whippet 50%
- McNab 30%
- Old English Sheepdog 5%
- Shetland Sheepdog 15%
- Silken Windhound 30%

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Follow-up Diagnostics to Consider

This is usually a retroactive diagnosis after a dog has an adverse reaction to a problem drug--however, genetic testing could help avoid a first reaction altogether.

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Treatment and Management Options

- Drugs that have been documented to cause problems in dogs with the ABCB1 variant include (from WSU):
- Macrocyclic lactones (including such drugs as ivermectin, milbemycin, moxidectin, and selamectin) - Route of application and dosage is crucial for the safety of treatment with macrocyclic lactones. Whereas all available macrocyclic lactones can safely be administered to ABCB1 mutant dogs at doses usually used for heartworm prevention, these dogs will experience neurological toxicity following a high dose regimen which has historically been used for demodectic mange treatment. **All FDA-approved heartworm prevention products licensed in the United States have been tested and found to be safe in dogs with the MDR1 variant.** (For study results, see label indications for specific trademark products.)
- ABCB1 heterozygote dogs can be regarded as having an intermediate macrocyclic lactone-sensitive phenotype. Currently, there is no specific and safe antidote available for the treatment of macrocyclic lactone-induced toxicosis. Therefore, treatment is solely based on symptomatic and supportive care. Care should also be taken to minimize non-direct exposure to these drugs (e.g. environmental or large-animal treatment).
- Loperamide (ImodiumTM) - At doses used to treat diarrhea, this drug will cause neurological toxicity in dogs with the MDR1 variant. This drug should be avoided in all dogs with the MDR1 variant.
- Acepromazine - Dose reductions are required for dogs with one or two copies of the MDR1 variant.
- Butorphanol - Dose reductions are required for dogs with one or two copies of the MDR1 variant.
- Chemotherapy Agents (vincristine, vinblastine, doxorubicin, paclitaxel)- Dose reductions are required for dogs with one or two copies of the MDR1 variant in order to avoid severe toxicity.
- Apomorphine - Dose reductions are required for dogs with one or two copies of the MDR1 variant, as it can cause central nervous system depression at standard doses.

More Information

Additional information regarding drugs that are known to be transported by the human or rodent forms of the protein encoded by the MDR1 gene with or without additional research in dogs can be found at https://vcpl.vetmed.wsu.edu/problem-drugs. Recommended dosage adjustments from WSU can be found at https://www.cliniciansbrief.com/article/how-should-i-treat-dogs-cats-mdr1-mutation.

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References

Neff MW, Robertson KR, Wong AK, et al. Breed distribution and history of canine mdr1-1Delta, a pharmacogenetic mutation that marks the emergence of breeds from the collie lineage. Proc Natl Acad Sci U S A. 2004;101(32):11725-11730. doi:10.1073/pnas.0402374101"

Deshpande D, Hill KE, Mealey KL, Chambers JP, Gieseg MA. The Effect of the Canine ABCB1-1Δ Mutation on Sedation after Intravenous Administration of Acepromazine. J Vet Intern Med. 2016;30(2):636-641. doi:10.1111/jvim.13827"

Geyer J, Janko C. Treatment of MDR1 mutant dogs with macrocyclic lactones. Curr Pharm Biotechnol. 2012;13(6):969-986. doi:10.2174/138920112800399301"

Mealey KL. Canine ABCB1 and macrocyclic lactones: heartworm prevention and pharmacogenetics. Vet Parasitol. 2008;158(3):215-222. doi:10.1016/j.vetpar.2008.09.009"

Mealey KL, Bentjen SA, Gay JM, Cantor GH. Ivermectin sensitivity in collies is associated with a deletion mutation of the mdr1 gene. Pharmacogenetics. 2001;11(8):727-733. doi:10.1097/00008571-200111000-00012"

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1 Notable Result

Degenerative Myelopathy, DM

How to interpret this result

Seymour has one copy of this variant in the SOD1A gene. Because this variant is inherited in an autosomal recessive manner (meaning dogs need two copies of the variant to develop the disease), Seymour is unlikely to develop Degenerative Myelopathy (DM) due to this variant.

Please note, this test is for the SOD1A variant. Embark does not test for the SOD1B variant (thought to only occur in Bernese Mountain Dogs) at this time. It is important to test Bernese Mountain Dogs for both variants as compound heterozygotes (one copy of SOD1A and one copy of SOD1B) can express the clinical disease.

While Seymour is not at risk for developing DM, he can pass this variant on to the next generation. If Seymour is intended for breeding, it is recommended to genotype any potential mates. You can email vetsupport@embarkvet.com to discuss with a genetic counselor how the genotype results should be applied to a breeding program.

What is Degenerative Myelopathy, DM?

A disease of mature dogs, Degenerative Myelopathy (DM) is a progressive degenerative disorder of the spinal cord that can cause muscle wasting and gait abnormalities. The initial clinical sign is proprioceptive ataxia in the pelvic limbs, and dogs with advanced DM progress to exhibit clinical signs of upper motor neuron paresis (UMN) and lower motor neuron disease (LMN) in all four limbs.

Any questions?

You can email vetsupport@embarkvet.com or call 1-855-203-8271 should you desire to speak with a genetic counselor for more information.

Variant Info

SOD1A

Recessive inheritance

1 copy of the variant

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Results Summary

To view COI and traits information, log into your account.

Auditory (2)

	Gene	Copies	Results
Deafness and Vestibular Syndrome of Dobermans, DVDob, DINGS	MYO7A	0	Clear
Early Onset Adult Deafness, EOAD - Rhodesian Ridgeback Variant	EPS8L2 Deletion Exon 12	0	Clear

Cardiac (4)

Dilated Cardiomyopathy	Gene	Copies	Results
Dilated Cardiomyopathy, DCM1 - Doberman Pinscher Variant 1	PDK4	0	Clear
Dilated Cardiomyopathy, DCM2 - Doberman Pinscher Variant 2	TTN	0	Clear

Other	Gene	Copies	Results
Cardiomyopathy and Juvenile Mortality - Belgian Shepherd Variant	YARS2	0	Clear
Long QT Syndrome - English Springer Spaniel Variant	KCNQ1	0	Clear

Endocrine (3)

Hypothyroidism	Gene	Copies	Results
Congenital Dyshormonogenic Hypothyroidism with Goiter - Shih Tzu Variant	SLC5A5	0	Clear
Congenital Hypothyroidism - Rat, Toy Fox, and Hairless Terrier Variant	TPO Exon 3	0	Clear
Congenital Hypothyroidism - Tenterfield Terrier Variant	TPO Exon 9	0	Clear

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Gastrointestinal (4)

Gastroenteropathy	Gene	Copies	Results
Lundehund Syndrome	LEPREL1	0	Clear

Malabsorptive Disorder	Gene	Copies	Results
Imerslund-Grasbeck Syndrome, Selective Cobalamin Malabsorption - Beagle Variant	CUBN Exon 8	0	Clear
Imerslund-Grasbeck Syndrome, Selective Cobalamin Malabsorption - Border Collie Variant	CUBN Exon 53	0	Clear
Inherited Selected Cobalamin Malabsorption with Proteinuria - Komondor Variant	CUBN	0	Clear

Hematologic (32)

Coagulopathy	Gene	Copies	Results
Bernard-Soulier Syndrome, BSS - Cocker Spaniel Variant	GP9	0	Clear
Congenital Macrothrombocytopenia - Cairn and Norfolk Terrier Variant	TUBB1 Exon 1	0	Clear
Factor IX Deficiency, Hemophilia B - Rhodesian Ridgeback Variant	F9 Exon 7	0	Clear
Factor IX Deficiency, Hemophilia B - Terrier Variant	F9 Exon 7	0	Clear
Factor VII Deficiency	F7 Exon 5	0	Clear
Factor VIII Deficiency, Hemophilia A - Boxer Variant	F8 Exon 10	0	Clear
Factor VIII Deficiency, Hemophilia A - German Shepherd Variant 1	F8 Exon 11	0	Clear
Factor VIII Deficiency, Hemophilia A - German Shepherd Variant 2	F8 Exon 1	0	Clear
Glanzmann's Thrombasthenia Type I - Great Pyrenees Variant	ITGA2B Exon 13	0	Clear
Glanzmann's Thrombasthenia Type I - Otterhound Variant	ITGA2B Exon 12	0	Clear

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	Gene	Copies	Results
May-Hegglin Anomaly - Pug Variant	MYH9	0	Clear
P2Y12 Receptor Platelet Disorder - Greater Swiss Mountain Dog Variant	P2Y12	0	Clear
Platelet Factor X Receptor Deficiency, Scott Syndrome - German Shepherd Dog Variant	TMEM16F	0	Clear
Prekallikrein Deficiency - Shih Tzu Variant	KLKB1 Exon 8	0	Clear
Thrombopathia - American Eskimo Dog Variant	RASGRP1 Exon 5	0	Clear
Thrombopathia - Basset Hound Variant	RASGRP1 Exon 5	0	Clear
Thrombopathia - Landseer Variant	RASGRP1 Exon 8	0	Clear
Von Willebrand Disease Type I, Type I vWD	VWF	0	Clear
Von Willebrand Disease Type II, Type II vWD - Pointer Variant	VWF	0	Clear
Von Willebrand Disease Type III, Type III vWD - Shetland Sheepdog Variant	VWF Exon 7	0	Clear
Von Willebrand Disease Type III, Type III vWD - Terrier Variant	VWF Exon 4	0	Clear

Red Blood Cell Abnormality	Gene	Copies	Results
Canine Elliptocytosis - Labrador Retriever Variant	SPTB Exon 30	0	Clear
Methemoglobinemia - Pomeranian Variant	CYB5R3	0	Clear
Pyruvate Kinase Deficiency - Basenji Variant	PKLR Exon 5	0	Clear
Pyruvate Kinase Deficiency - Beagle Variant	PKLR Exon 7	0	Clear
Pyruvate Kinase Deficiency - Labrador Retriever Variant	PKLR Exon 7	0	Clear
Pyruvate Kinase Deficiency - Pug Variant	PKLR Exon 7	0	Clear
Pyruvate Kinase Deficiency - Terrier Variant	PKLR Exon 10	0	Clear

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White Blood Cell Abnormality	Gene	Copies	Results
Canine Leukocyte Adhesion Deficiency Type I, CLAD I - Setter Variant	ITGB2 Exon 3	0	Clear
Canine Leukocyte Adhesion Deficiency Type III, CLAD III - German Shepherd Variant	FERMT3	0	Clear
Trapped Neutrophil Syndrome, TNS	VPS13B Exon 19	0	Clear

Other	Gene	Copies	Results
Ligneous Membranitis, LM - Scottish Terrier Variant	PLG	0	Clear

Immunologic (6)

	Gene	Copies	Results
Complement 3 Deficiency, C3 Deficiency - Brittany Variant	C3	0	Clear
Severe Combined Immunodeficiency, SCID - Terrier Variant	PRKDC	0	Clear
Severe Combined Immunodeficiency, SCID - Wetterhoun Variant	RAG1	0	Clear
Shar-Pei Autoinflammatory Disease, SPAID, Shar-Pei Fever	MTBP	0	Clear
X-linked Severe Combined Immunodeficiency, X-SCID - Basset Hound Variant	IL2RG Exon 1	0	Clear
X-linked Severe Combined Immunodeficiency, X-SCID - Corgi Variant	IL2RG	0	Clear

Integument (18)

Collagen Abnormality	Gene	Copies	Results
Dystrophic Epidermolysis Bullosa - Central Asian Shepherd Dog Variant	COL7A1	0	Clear
Dystrophic Epidermolysis Bullosa - Golden Retriever Variant	COL7A1 Exon 68	0	Clear

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	Gene	Copies	Results
Ehlers Danlos - Doberman Pinscher Variant	ADAMTS2	0	Clear
Musladin-Lueke Syndrome, MLS - Beagle Variant	ADAMTSL2 Exon 7	0	Clear

Keratin Abnormality	**Gene**	**Copies**	**Results**
Congenital Keratoconjunctivitis Sicca and Ichthyosiform Dermatosis, Dry Eye Curly Coat Syndrome, CKCSID - Cavalier King Charles Spaniel Variant	FAM83H	0	Clear
Focal Non-Epidermolytic Palmoplantar Keratoderma, Pachyonychia Congenita - Dogue de Bordeaux Variant	KRT16 Exon 6	0	Clear
Hereditary Footpad Hyperkeratosis - Rottweiler Variant	DSG1	0	Clear
Hereditary Footpad Hyperkeratosis - Terrier and Kromfohrlander Variant	FAM83G	0	Clear
Hereditary Nasal Parakeratosis, HNPK - Labrador Retriever Variant	SUV39H2	0	Clear
Ichthyosis, Epidermolytic Hyperkeratosis - Terrier Variant	KRT10 Intron 5	0	Clear
Ichthyosis, ICH1 - Golden Retriever Variant	PNPLA1 Exon 8	0	Clear
Ichthyosis - American Bulldog Variant	NIPAL4 Exon 6	0	Clear
Ichthyosis - Great Dane Variant	SLC27A4	0	Clear

Other	**Gene**	**Copies**	**Results**
Bald Thigh Syndrome - Greyhound Variant	IGFBP5	0	Clear
Ectodermal Dysplasia, Skin Fragility Syndrome - Chesapeake Bay Retriever Variant	PKP1 Intron 1	0	Clear
Lethal Acrodermatitis, LAD - Bull Terrier Variant	MKLN1	0	Clear

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Oculocutaneous Albinism, OCA - Small Breed Variant	SLC45A2	0	Clear
X-linked Ectodermal Dysplasia, Anhidrotic Ectodermal Dysplasia, XHED - German Shepherd Dog Variant	EDA	0	Clear

Metabolic (33)

Enzyme Deficiency	Gene	Copies	Results
Hypocatalasia, Acatalasemia - Beagle Variant	CAT	0	Clear
L-2-Hydroxyglutaricaciduria, L2HGA - Staffordshire Bull Terrier Variant	L2HGDH	0	Clear
Pyruvate Dehydrogenase Deficiency - Spaniel Variant	PDP1	0	Clear

Storage Disease	Gene	Copies	Results
Canine Fucosidosis - English Springer Spaniel Variant	FUCA1	0	Clear
GM1 Gangliosidosis - Alaskan Husky Variant	GLB1 Exon 15	0	Clear
GM1 Gangliosidosis - Portuguese Water Dog Variant	GLB1 Exon 2	0	Clear
GM1 Gangliosidosis - Shiba Inu Variant	GLB1 Exon 15	0	Clear
GM2 Gangliosidosis - Japanese Chin Variant	HEXA	0	Clear
GM2 Gangliosidosis - Poodle Variant	HEXB Exon 3	0	Clear
Globoid Cell Leukodystrophy, Krabbe Disease - Terrier Variant	GALC Exon 5	0	Clear
Glycogen Storage Disease Type IA, Von Gierke Disease, GSD IA - Maltese Variant	G6PC	0	Clear
Glycogen Storage Disease Type II, Pompe's Disease, GSD II - Finnish and Swedish Lapphund, Lapponian Herder Variant	GAA Exon 15	0	Clear
Glycogen Storage Disease Type IIIA, GSD IIIA - Curly Coated Retriever Variant	AGL GDE	0	Clear

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Glycogen storage disease Type VII, Phosphofructokinase Deficiency, PFK Deficiency - Wachtelhund Variant	PFKM Exon 8	0	Clear
Glycogen storage disease Type VII, Phosphofructokinase Deficiency, PFK Deficiency - Whippet and English Springer Spaniel Variant	PFKM Exon 21	0	Clear
Lagotto Storage Disease	ATG4D Exon 10	0	Clear
Late-Onset Neuronal Ceroid Lipofuscinosis, NCL12 - Australian Cattle Dog Variant	ATP13A2	0	Clear
Mucopolysaccharidosis IIIB, Sanfilippo Syndrome Type B, MPS IIIB - Schipperke Variant	NAGLU	0	Clear
Mucopolysaccharidosis Type IIIA, Sanfilippo Syndrome Type A, MPS IIIA - Dachshund Variant	SGSH	0	Clear
Mucopolysaccharidosis Type IIIA, Sanfilippo Syndrome Type A, MPS IIIA - New Zealand Huntaway Variant	SGSH	0	Clear
Mucopolysaccharidosis Type VII, Sly Syndrome, MPS VII - German Shepherd Variant	GUSB	0	Clear
Mucopolysaccharidosis Type VII, Sly Syndrome, MPS VII - Terrier Brasileiro Variant	GUSB	0	Clear
Neuronal Ceroid Lipofuscinosis 1, NCL1 - Dachshund Variant	PPT1 Exon 8	0	Clear
Neuronal Ceroid Lipofuscinosis 10, NCL10 - American Bulldog Variant	CTSD Exon 5	0	Clear
Neuronal Ceroid Lipofuscinosis 2, NCL2 - Dachshund Variant	TPP1 Exon 4	0	Clear
Neuronal Ceroid Lipofuscinosis 5, NCL5 - Border Collie and Australian Cattle Dog Variant	CLN5 Exon 4	0	Clear
Neuronal Ceroid Lipofuscinosis 5, NCL5 - Golden Retriever Variant	CLN5 Exon 4	0	Clear
Neuronal Ceroid Lipofuscinosis 6, NCL6 - Australian Shepherd Variant	CLN6 Exon 7	0	Clear
Neuronal Ceroid Lipofuscinosis 7, NCL7 - Chihuahua and Chinese Crested Variant	MFSD8	0	Clear

	Gene	Copies	Results
Neuronal Ceroid Lipofuscinosis 8, NCL8 - Australian Shepherd and German Shorthaired Pointer Variant	CLN8	0	Clear
Neuronal Ceroid Lipofuscinosis 8, NCL8 - English Setter Variant	CLN8 Exon 2	0	Clear
Neuronal Ceroid Lipofuscinosis 8, NCL8 - Saluki Variant	CLN8	0	Clear
Neuronal Ceroid Lipofuscinosis, Cerebellar Ataxia, NCL4A - American Staffordshire Terrier Variant	ARSG Exon 2	0	Clear

Muscular (13)

Movement Disorder	Gene	Copies	Results
Myotonia Congenita - Australian Cattle Dog Variant	CLCN1 Exon 23	0	Clear
Myotonia Congenita - Miniature Schnauzer Variant	CLCN1 Exon 7	0	Clear

Muscular Dystrophy	Gene	Copies	Results
Limb Girdle Muscular Dystrophy - Boston Terrier Variant	SGCD	0	Clear
Muscular Dystrophy - Cavalier King Charles Spaniel Variant 1	DMD	0	Clear
Muscular Dystrophy - Golden Retriever Variant	DMD	0	Clear
Ullrich-like Congenital Muscular Dystrophy - Labrador Retriever Variant 1	COL6A3 Exon 10	0	Clear

Myopathy	Gene	Copies	Results
Centronuclear Myopathy, CNM - Labrador Retriever Variant	PTPLA	0	Clear
Exercise-Induced Collapse, EIC	DNM1	0	Clear
Inflammatory Myopathy - Dutch Shepherd Variant	SLC25A12	0	Clear

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Inherited Myopathy of Great Danes	BIN1	0	Clear
Myotubular Myopathy 1, X-linked Myotubular Myopathy, XL-MTM - Labrador Retriever Variant	MTM1 Exon 7	0	Clear
Nemaline Myopathy - American Bulldog Variant	NEB	0	Clear

Other	Gene	Copies	Results
Myostatin Deficiency, Bully Whippet Syndrome	MSTN	0	Clear

Neurologic (32)

Brain or Seizure Disorder	Gene	Copies	Results
Alaskan Husky Encephalopathy, Subacute Necrotizing Encephalomyelopathy	SLC19A3 Exon 2	0	Clear
Alexander Disease - Labrador Retriever Variant	GFAP Exon 4	0	Clear
Benign Familial Juvenile Epilepsy, Remitting Focal Epilepsy - Lagotto Romagnolo Variant	LGI2 Exon 8	0	Clear
Cerebellar Abiotrophy, Neonatal Cerebellar Cortical Degeneration, NCCD - Beagle Variant	SPTBN2	0	Clear
Cerebellar Hypoplasia - Eurasier Variant	VLDLR	0	Clear
Hereditary Ataxia, Cerebellar Degeneration - Old English Sheepdog and Gordon Setter Variant	RAB24 Exon 1	0	Clear
Neonatal Encephalopathy with Seizures, NEWS - Poodle Variant	ATF2	0	Clear
Progressive Early-Onset Cerebellar Ataxia - Finnish Hound Variant	SEL1L	0	Clear
Spinocerebellar Ataxia with Myokymia and/or Seizures - Terrier Variant 2	KCNJ10	0	Clear
Spinocerebellar Ataxia, Late-Onset Ataxia, LoSCA - Terrier Variant 1	CAPN1	0	Clear

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	Gene	Copies	Results
Spongy Degeneration with Cerebellar Ataxia 1, SDCA1, SeSAME/EAST Syndrome - Shepherd Variant 1	KCNJ10	0	Clear
Spongy Degeneration with Cerebellar Ataxia 2, SDCA2 - Shepherd Variant 2	ATP1B2	0	Clear

Movement Disorder	Gene	Copies	Results
Degenerative Myelopathy, DM	SOD1A	1	Notable
Hypomyelination and Tremors - Weimaraner Variant	FNIP2	0	Clear
Juvenile Myoclonic Epilepsy - Rhodesian Ridgeback Variant	DIRAS1	0	Clear
Progressive Neuronal Abiotrophy, Canine Multiple System Degeneration, CMSD - Chinese Crested Variant	SERAC1	0	Clear
Progressive Neuronal Abiotrophy, Canine Multiple System Degeneration, CMSD - Kerry Blue Terrier Variant	SERAC1	0	Clear
Shaking Puppy Syndrome, X-linked Generalized Tremor Syndrome - English Springer Spaniel Variant	PLP1	0	Clear

Narcolepsy	Gene	Copies	Results
Narcolepsy - Dachshund Variant	HCRTR2	0	Clear
Narcolepsy - Doberman Pinscher Variant	HCRTR2	0	Clear
Narcolepsy - Labrador Retriever Variant	HCRTR2	0	Clear

Neurodegenerative Disorder	Gene	Copies	Results
Fetal-Onset Neonatal Neuroaxonal Dystrophy - Giant Schnauzer Variant	MFN2	0	Clear
Neuroaxonal Dystrophy, NAD - Rottweiler Variant	VPS11	0	Clear
Neuroaxonal Dystrophy, NAD - Spanish Water Dog Variant	TECPR2	0	Clear

Seymour

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Neuropathy	Gene	Copies	Results
Alaskan Malamute Polyneuropathy, AMPN	NDRG1	0	Clear
Demyelinating Polyneuropathy - Miniature Schnauzer Variant	SBF2/MTRM13	0	Clear
Juvenile Laryngeal Paralysis and Polyneuropathy, Polyneuropathy with Ocular Abnormalities and Neuronal Vacuolation, POANV - Rottweiler Variant	RAB3GAP1	0	Clear
Juvenile-Onset Polyneuropathy, Leonberger Polyneuropathy 1, LPN1	ARHGEF10 Exon 17	0	Clear
Juvenile-Onset Polyneuropathy, Leonberger Polyneuropathy 2, LPN2	GJA9	0	Clear
Laryngeal Paralysis - Miniature Bull Terrier Variant	RAPGEF6	0	Clear

Sensory Neuropathy	Gene	Copies	Results
Hereditary Sensory Autonomic Neuropathy, Acral Mutilation Syndrome, AMS - Spaniel and Pointer Variant	GDNF-AS	0	Clear
Sensory Neuropathy - Border Collie Variant	FAM134B	0	Clear

Neuromuscular (7)

Junctionopathy	Gene	Copies	Results
Congenital Myasthenic Syndrome, CMS - Golden Retriever Variant	COLQ Exon 13	0	Clear
Congenital Myasthenic Syndrome, CMS - Heideterrier Variant	CHRNE	0	Clear
Congenital Myasthenic Syndrome, CMS - Jack Russell Terrier Variant	CHRNE Exon 7	0	Clear
Congenital Myasthenic Syndrome, CMS - Labrador Retriever Variant	COLQ Exon 14	0	Clear
Congenital Myasthenic Syndrome, CMS - Old Danish Pointing Dog Variant	CHAT Exon 6	0	Clear

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Movement Disorder	Gene	Copies	Results
Episodic Falling Syndrome - Cavalier King Charles Spaniel Variant	BCAN Exons 1-4	0	Clear
Paroxysmal Dyskinesia, PxD - Soft Coated Wheaten Terrier Variant	PIGN	0	Clear

Ophthalmologic (31)

Glaucoma	Gene	Copies	Results
Goniodysgenesis and Glaucoma, Pectinate Ligament Dysplasia, PLD - Border Collie Variant	OLFML3	0	Clear
Primary Open Angle Glaucoma and Primary Lens Luxation - Chinese Shar-Pei Variant	ADAMTS17	0	Clear
Primary Open Angle Glaucoma - Basset Fauve de Bretagne Variant	ADAMTS17	0	Clear
Primary Open Angle Glaucoma - Beagle Variant	ADAMTS10	0	Clear
Primary Open Angle Glaucoma - Norwegian Elkhound Variant	ADAMTS10	0	Clear

Iris or Lens	Gene	Copies	Results
Hereditary Cataracts, Early-Onset Cataracts, Juvenile Cataracts - Australian Shepherd Variant	HSF4	0	Clear
Primary Lens Luxation	ADAMTS17	0	Clear

Retinopathy	Gene	Copies	Results
Achromatopsia - German Shepherd Variant	CNGA3 Exon 7	0	Clear
Achromatopsia - Labrador Retriever Variant	CNGA3 Exon 7	0	Clear
Autosomal Dominant Progressive Retinal Atrophy - English Mastiff and Bullmastiff Variant	RHO Exon 1	0	Clear
Canine Multifocal Retinopathy, cmr1	BEST1/VMD2 Exon 2	0	Clear

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	Gene	Copies	Results
Canine Multifocal Retinopathy, cmr2 - Coton de Tulear Variant	BEST1/VMD2 Exon 5	0	Clear
Canine Multifocal Retinopathy, cmr3 - Finnish and Swedish Lapphund, Lapponian Herder Variant	BEST1/VMD2 Exon 10	0	Clear
Collie Eye Anomaly, Choroidal Hypoplasia, CEA	NHEJ1 Intron 4	0	Clear
Congenital Stationary Night Blindness - Beagle Variant	LRIT3	0	Clear
Congenital Stationary Night Blindness - Briard Variant	RPE65	0	Clear
Day Blindness, Cone Degeneration, Achromatopsia - Alaskan Malamute Variant	CNGB3 Deletion	0	Clear
Day Blindness, Cone Degeneration, Achromatopsia - German Shorthaired Pointer Variant	CNGB3 Exon 6	0	Clear
Golden Retriever Progressive Retinal Atrophy 1, GR-PRA1	SLC4A3 Exon 16	0	Clear
Golden Retriever Progressive Retinal Atrophy 2, GR-PRA2	TTC8 Exon 8	0	Clear
Macular Corneal Dystrophy, MCD - Labrador Retriever Variant	CHST6	0	Clear
Progressive Retinal Atrophy, CNGA - Shetland Sheepdog Variant	CNGA1 Exon 9	0	Clear
Progressive Retinal Atrophy, Cone-Rod Dystrophy 1, crd1 - American Staffordshire Terrier Variant	PDE6B	0	Clear
Progressive Retinal Atrophy, Cone-Rod Dystrophy 4, crd4/cord1	RPGRIP1 Exon 2	0	Clear
Progressive Retinal Atrophy, PRA1 - Papillon Variant	CNGB1	0	Clear
Progressive Retinal Atrophy, PRA3 - Tibetan Spaniel and Terrier Variant	FAM161A	0	Clear
Progressive Retinal Atrophy, Progressive Rod-Cone Degeneration, prcd	PRCD Exon 1	0	Clear
Progressive Retinal Atrophy, Rod-Cone Dysplasia 1, rcd1 - Irish Setter Variant	PDE6B Exon 21	0	Clear
Progressive Retinal Atrophy, Rod-Cone Dysplasia 3, rcd3 - Corgi Variant	PDE6A	0	Clear

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	Gene	Copies	Results
Progressive Retinal Atrophy - Basenji Variant	SAG	0	Clear
X-Linked Progressive Retinal Atrophy 1, XL-PRA1 - Samoyed and Husky Variant	RPGR Exon 15	0	Clear

Oral Cavity (4)

Developmental Disorder	Gene	Copies	Results
Cleft Lip and/or Cleft Palate - Nova Scotia Duck Tolling Retriever Variant	ADAMTS20	0	Clear

Tooth Structure Defect	Gene	Copies	Results
Autosomal Recessive Amelogenesis Imperfecta, Familial Enamel Hypoplasia - Italian Greyhound Variant	ENAM	0	Clear
Autosomal Recessive Amelogenesis Imperfecta, Familial Enamel Hypoplasia - Parson Russell Terrier Variant	ENAM	0	Clear
Raine Syndrome, Canine Dental Hypomineralization Syndrome - Border Collie Variant	FAM20C	0	Clear

Personalized Medicine (3)

	Gene	Copies	Results
Alanine Aminotransferase Activity	GPT	0	Clear
MDR1 Drug Sensitivity	ABCB1	1	At risk
Malignant Hyperthermia	RYR1	0	Clear

Pulmonary (4)

	Gene	Copies	Results
Neonatal Interstitial Lung Disease - Airedale Terrier Variant	LAMP3	0	Clear

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	Gene	Copies	Results
Primary Ciliary Dyskinesia, PCD - Alaskan Malamute Variant	NME5	0	Clear
Primary Ciliary Dyskinesia, PCD - Old English Sheepdog Variant	CCDC39	0	Clear
Recurrent Inflammatory Pulmonary Disease, RIPD - Rough Collie Variant	AKNA	0	Clear

Skeletal (10)

Chondrodystrophy	Gene	Copies	Results
Chondrodystrophy and Intervertebral Disc Disease, CDDY/IVDD, Type I IVDD - Retrogene	FGF4 - chr12	0	Clear
Chondrodystrophy - Norwegian Elkhound and Karelian Bear Dog Variant	ITGA10	0	Clear
Oculoskeletal Dysplasia 2, Dwarfism-Retinal Dysplasia 2, drd2, OSD2 - Samoyed Variant	COL9A2 5' UTR	0	Clear
Osteochondrodysplasia, Skeletal Dwarfism - Miniature Poodle Variant	SLC13A1	0	Clear
Skeletal Dysplasia 2, SD2 - Labrador Retriever Variant	COL11A2	0	Clear

Decreased Bone Strength	Gene	Copies	Results
Hereditary Vitamin D-Resistant Rickets - Pomeranian Variant	VDR Exon 4	0	Clear
Osteogenesis Imperfecta, Brittle Bone Disease - Beagle Variant	COL1A2	0	Clear
Osteogenesis Imperfecta, Brittle Bone Disease - Dachshund Variant	SERPINH1 Exon 5	0	Clear
Osteogenesis Imperfecta, Brittle Bone Disease - Golden Retriever Variant	COL1A1 Exon 18	0	Clear

Other	Gene	Copies	Results
Craniomandibular Osteopathy, CMO - Terrier and Australian Shepherd Variant	SLC37A2 Exon 15	0	Clear

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Urogenital (14)

Nephropathy	Gene	Copies	Results
Autosomal Recessive Hereditary Nephropathy, Familial Nephropathy, ARHN - Cocker Spaniel Variant	COL4A4 Exon 3	0	Clear
Autosomal Recessive Hereditary Nephropathy, Familial Nephropathy, ARHN - English Springer Spaniel Variant	COL4A4 Exon 30	0	Clear
Fanconi Syndrome - Basenji Variant	FAN1	0	Clear
Polycystic Kidney Disease, PKD - Bull Terrier Variant	PKD1 Exon 29	0	Clear
Protein Losing Nephropathy, PLN - Soft Coated Wheaten and Airedale Terrier Variant	NPHS1	0	Clear
X-Linked Hereditary Nephropathy, XLHN - Samoyed Variant 2	COL4A5 Exon 35	0	Clear

Urolithiasis	Gene	Copies	Results
2,8-Dihydroxyadenine Urolithiasis, 2,8-DHA Urolithiasis - American Indian Dog Variant	APRT Exon 3	0	Clear
Cystinuria Type I-A - Newfoundland Variant	SLC3A1 Exon 2	0	Clear
Cystinuria Type II-A - Australian Cattle Dog Variant	SLC3A1 Exon 6	0	Clear
Cystinuria Type II-B - Miniature Pinscher Variant	SLC7A9 Exon 9	0	Clear
Hyperuricosuria and Hyperuricemia or Urolithiasis, HUU	SLC2A9 Exon 5	0	Clear
Primary Hyperoxaluria - Coton de Tulear Variant	AGXT Exon 2	0	Clear

Other	Gene	Copies	Results
Persistent Mullerian Duct Syndrome, PMDS - Miniature and Standard Schnauzer Variant	AMHR2	0	Clear
Renal Cystadenocarcinoma and Nodular Dermatofibrosis, RCND - German Shepherd Dog Variant	FLCN	0	Clear

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Glossary

Key Terms

Increased Risk Result

The dog is at risk for showing clinical signs (phenotype) of a given condition. For recessive conditions, this means a dog has inherited two copies of an associated variant. For dominant, codominant, and additive conditions, this means a dog has inherited at least one copy of the variant. X-linked conditions will vary based on sex of the dog.

A dog's breed(s) and genetic background are also considered in this assessment. Genetic testing is an assessment of risk and not a clinical diagnosis, and not all dogs in this category will develop clinical signs.

Notable Result

A result may be notable for several reasons. The variant may not induce a disease state but rather inform patient care (this may include the tests listed under Personalized Medicine). The dog may have only one copy of a variant with a recessive mode of inheritance (meaning the dog is a carrier and is not expected to show the phenotype associated with the variant). The impact of the variant may also be influenced by a dog's breed(s). Based on the available research within the breed or related breeds, you will see more specific text within the results.

Clear Result

A dog with two healthy copies of a gene sequence is not at risk for developing the associated disease due to that variant. Many diseases can manifest as a result of other unknown genetic variants and/or environmental factors.

Variant

An alteration in the DNA with the potential to cause a change in phenotype (i.e. disease). A report may state that the dog has zero, one, or two copies of the variant for which we test. The term "variant" may be used interchangeably with "mutation."

Genotype

The genetic code related to the variant being present or absent in the dog's DNA.

Phenotype

The physical impact or appearance directed by the genotype. The phenotype is often described as an expression of the genotype.

Complex Phenotype

The condition, appearance, or other physical expression of the genotype controlled by both genetic and environmental factors.

Penetrance

Proportion of dogs with a particular genotype that expresses the associated phenotype. There are two types of penetrance.

1. Incomplete penetrance means that not all dogs with the genotype will develop the clinical signs of the phenotype.

2. Complete penetrance means that all dogs with the genotype will develop the clinical signs of the phenotype.

Carrier

This term has traditionally been used to describe a dog that has one copy of the variant but is not expected to show the phenotype associated with the variant (this is applicable to variants with a recessive mode of inheritance (MOI) as described below). If used in a breeding pair, a carrier may pass the variant to its litter.

At-risk

This indicates that the dog may manifest the disease and generally is used when a dog has two copies of the variant (but this depends on the MOI).

Embark uses the term "at-risk" and not "affected" because genetic testing is an assessment of risk and not a clinical diagnosis.

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Linkage Disequilibrium Test

When a causal variant cannot be identified or when the variant is incompatible with the genotyping platform constraints, allelic association or linkage disequilibrium (LD) tests can be utilized. This is typically done to assist dog breeders in selectively breeding out a deleterious condition. LD tests are based on a statistical association between two loci that are physically very close in the DNA. The coupling of the chosen proxy marker to the causal variant is known mathematically for the most relevant populations.

LD-based tests have a slightly increased incidence of false positives and false negatives, which are test-specific and known. Embark offers limited numbers of these tests. Embark continuously works to refine LD-based tests by assaying the direct variant in a subset of dogs using alternative methods. These inputs help to refine the tests over time.

Provisional Result

Embark combines random sampling and sequencing with the use of blinded controls to confirm that each test is performing to standard at >99% genotyping accuracy and reproducibility. Our standard health tests have been validated using known heterozygous and homozygous samples to ensure design accuracy and use multiple probes per condition to ensure reproducibility. Provisional tests are for rare disorders for which DNA samples from carrier and/or at-risk individuals are not available for calculating test reliability, or for structural variants where more testing is needed to ensure the same level of accuracy.

If you have access to DNA from carrier or at-risk individuals and are interested in helping us validate a test, please contact us at vetsupport@embarkvet.com

Modes of Inheritance

Recessive

A dog is thought to need two copies of a variant to be considered at-risk for the clinical disease or to have the visible phenotype for traits. This may apply to autosomal or X-linked variants, however. Read below for additional details regarding X-linked variants.

Dominant

A dog is thought to need only one copy of the variant to be considered at-risk for the clinical disease or to have the visible phenotype for traits.

Codominant/Additive

In general, these terms are used to describe variants in which dogs with one copy of the variant have a different phenotype compared to dogs with zero or two copies of the variant (although there is a slight difference between the two terms).

X-linked

The variant resides on the X chromosome, and male dogs need just one copy of the variant to be considered at-risk. For recessively inherited X-linked conditions, female dogs typically require two copies of the variant to be considered at-risk. Female dogs who have one copy of a recessively inherited X-linked variant are often referred to as carriers, but they can exhibit signs of disease that range from clinically asymptomatic to fully affected. This is due to a normal phenomenon known as X-chromosome inactivation, where one X chromosome is silenced in each cell.

Weight

The Embark DNA test provides a genetic size based not just on breed ancestry but on over a dozen genes known to influence a dog's weight, as well as sex and breed-specific modifiers.

Our algorithm explains over 85% of the variance in healthy adult weight. However, due to a few as-yet-undiscovered genes and genetic interactions that affect size, this algorithm sometimes under or over-predicts weight.

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Genetic Age

Dogs age at very different rates due to a number of genetic and environmental factors. Embark's genetic age calculates how old a dog would be if he or she were aging at an average human rate (using humans in the USA as the baseline). This measure is more personalized than "one dog year = seven human years".

View the patient's profile see the personalized genetic age table for this dog.

We start by asking the dog's approximate calendar age. We then calculate genetic age by factoring a dog's breed composition along with information from genes that affect size, sex, and the dog's inbreeding coefficient (COI).

Impact of Breed

When determining whether or not a variant is expected to have a clinical impact for a breed, we have taken into account research either published, internal, or otherwise presented by a subject matter authority as our primary criteria. So, while a dog may have the variant associated with a disease (one or two copies for dominant variants and two copies for autosomal recessive variants), he or she may not be known to be at significant clinical risk from that variant.

Based on the available research within the breed or highly related breeds, you may see text similar to the following options:

1. This genetic variant is not likely to significantly increase the risk that this dog will develop the clinical disease.

2. This genetic variant is associated with an increased risk that this dog will develop the clinical disease.

3. We do not know whether this variant increases the risk that this dog will develop the clinical disease.

Embark is continuing to explore the relationship of genotype to phenotype, and risk assessment may be updated as more data is reviewed. You can contact vetsupport@embarkvet.com or call 1-855-203-8271 to report any clinical diagnoses.